

We claim:

1. An isolated nucleic acid molecule encoding a CARD-containing polypeptide, or a CARD, NB-ARC, ANGIO-R, LRR or SAM domain therefrom, selected from:

5 (a) DNA encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NOS: 12, 168, 188, 170, 172, 174, 176, 97, 99, 101, 103, 178, 180, 182, 184, 86 and 90; and
(b) DNA that hybridizes to the DNA of (a)
10 under moderately stringent conditions, wherein said DNA encodes a biologically active polypeptide.

2. The nucleic acid molecule of claim 1, wherein the nucleotide sequence of said nucleic acid 15 molecule comprises any of SEQ ID NOS:11, 167, 187, 169, 171, 173, 175, 96, 98, 100, 102, 177, 179, 181, 183, 85 and 89.

3. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule is cDNA.

20 4. A vector containing the nucleic acid molecule of claim 1.

5. Recombinant cells containing the nucleic acid molecule of claim 1.

25 6. An isolated oligonucleotide comprising at least 15 contiguous nucleotides of the nucleic acid molecule of claim 2.

7. An oligonucleotide according to claim 6, wherein said oligonucleotide is labeled with a detectable marker.

8. A kit for detecting the presence of CARD-5 encoding nucleic acid molecule comprising at least one oligonucleotide according to claim 6.

9. An isolated CARD-containing polypeptide, or a CARD, NB-ARC, ANGIO-R, LRR or SAM domain therefrom, comprising an amino acid sequence at least 70% identical 10 to the amino acid sequence set forth in any of SEQ ID NOS:12, 168, 188, 170, 172, 174, 176, 97, 99, 101, 103, 178, 180, 182, 184, 86 and 90.

10. The CARD-containing polypeptide of claim 15 9, wherein said polypeptide is encoded by a nucleotide sequence set forth as any of SEQ ID NOS:11, 167, 187, 169, 171, 173, 175, 96, 98, 100, 102, 177, 179, 181, 183, 85 and 89.

11. A peptide, comprising at least 10 20 contiguous amino acids of the polypeptide of claim 9.

12. A method of producing a CARD-containing polypeptide comprising expressing the cDNA of claim 3 *in vitro* or in a cell under conditions suitable for expression of said polypeptide, wherein said cells are 25 selected from the group consisting of bacteria cells, yeast cells, plant cells, animal cells, mammalian cells and insect cells.

13. An isolated anti-CARD antibody having specific reactivity with the CARD-containing polypeptide of claim 9.

14. The antibody of claim 13, wherein said 5 antibody is a monoclonal antibody.

15. A cell line producing the monoclonal antibody of claim 14.

16. The antibody of claim 13, wherein said antibody is a polyclonal antibody.

10 17. A method for identifying a nucleic acid molecule encoding a CARD-containing polypeptide, said method comprising:

15 contacting a sample containing nucleic acids with an oligonucleotide according to claim 6, wherein said contacting is effected under high stringency hybridization conditions, and identifying a nucleic acid molecule which hybridizes thereto.

18. A method for detecting the presence of a CARD-containing polypeptide in a sample, said method 20 comprising contacting a test sample with an antibody according to claim 13, detecting the presence of an antibody:CARD complex, and thereby detecting the presence of a human CARD-containing polypeptide in said test sample.

19. A method of identifying a CARD-associated polypeptide (CAP) comprising the steps of:

(a) contacting the CARD-containing polypeptide of claim 9 with a candidate CAP;

5 (b) detecting association of said CARD-containing polypeptide with said CAP.

20. A method of identifying an effective agent that alters the association of a CARD-containing polypeptide with a CARD-associated polypeptide (CAP), comprising the steps of:

(a) contacting the CARD-containing polypeptide of claim 9 and said CAP under conditions that allow said CARD-containing polypeptide and said CAP to associate with an agent suspected of being able to alter the association of said CARD-containing polypeptide and said CAP; and

15 (b) detecting the altered association of said CARD-containing polypeptide and said CAP, wherein said altered association identifies an effective agent.

20 21. A method of identifying an effective agent that alters the association of a CARD-containing polypeptide with a CARD-associated polypeptide (CAP), comprising the steps of:

25 (a) contacting the CARD-containing polypeptide of claim 9 and said CAP under conditions that allow said CARD-containing polypeptide and said CAP to associate with an agent suspected of being able to alter the

association of said CARD-containing polypeptide and said CAP; and

5 (b) detecting the altered association of said CARD-containing polypeptide and said CAP, wherein said altered association identifies an effective agent, wherein said CAP is a CARD-containing polypeptide according to claim 9.

22. A method of altering the level of a biochemical process modulated by a CARD-containing 10 polypeptide, comprising the steps of:

(a) introducing the nucleic acid molecule of claim 1 into a cell; and

15 (b) expressing said nucleic acid molecule in said cell, whereby the expression of said nucleic acid alters the level of a biochemical process modulated by a CARD-containing polypeptide.

23. The method of claim 22, wherein said biochemical process modulated by a CARD-containing 20 polypeptide is selected from the group consisting of apoptosis, NF- κ B induction, cytokine processing, cJun N-terminal kinase induction, caspase-mediated proteolysis, transcription, inflammation and cell adhesion.

24. A method of altering the level of a biochemical process modulated by a CARD-containing polypeptide, comprising introducing an antisense nucleotide sequence into a cell, wherein said antisense nucleotide sequence specifically hybridizes to a nucleic acid molecule encoding the CARD-containing polypeptide of claim 11, whereby hybridization reduces or inhibits the expression of said CARD-containing polypeptide in said cell.

10 25. A method of altering the level of a biochemical process modulated by a CARD-containing polypeptide, comprising contacting a sample with an agent that effectively alters the association of the CARD-containing polypeptide of claim 9 with a CARD-associated 15 polypeptide, whereby the level of a biochemical process modulated by a CARD-containing polypeptide is altered.

20 26. A method of diagnosing or predicting clinical prognosis of a pathology characterized by an increased or decreased level of a CARD-containing polypeptide in a subject, comprising the steps of:

- (a) obtaining a test sample from the subject;
- (b) contacting said test sample with an agent that can bind the CARD-containing polypeptide of claim 9 under suitable conditions, which allow specific binding of said agent to said CARD-containing polypeptide; and
- (c) comparing the amount of said specific binding in said test sample with the amount of specific binding in a reference sample, wherein

an increased or decreased amount of said specific binding in said test sample as compared to said reference sample is diagnostic or predictive of clinical prognosis of a pathology.

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27. A composition comprising a compound selected from the group consisting of a CARD-containing polypeptide, a functional fragment therefrom, and an anti-CARD antibody; and a pharmaceutically acceptable carrier.

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28. A method of treating a pathology characterized by abnormal cell proliferation, abnormal cell death, or inflammation, said method comprising administering to an individual an effective amount of the composition of claim 27.

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29. A chimeric polypeptide comprising a domain selected from the group consisting of SEQ ID NOS:168, 170, 172, 174, 176, 178, 180, 182 and 184.

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30. A method of identifying an effective agent that modulates an activity of a NB-ARC domain of a CARD-containing polypeptide, comprising the steps of:

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(a) contacting a polypeptide comprising an NB-ARC domain set forth as either of SEQ ID NOS:174 or 180 with an agent known or suspected of modulating an activity of an NB-ARC domain; and

(b) measuring the activity of the NB-ARC domain, whereby an increase or decrease of said activity identifies said agent as an agent that

modulates the activity of the NB-ARC domain of
said CARD-containing polypeptide;
wherein the activity of the NB-ARC domain of said CARD-
containing polypeptide is selected from homo-
5 oligomerization, hetero-oligomerization, nucleotide
hydrolysis, and nucleotide binding.